Search Notes: 10/572,638

DATE: Thursday, December 16, 2010

Set Side	Name by Side	Query	Hit Count	Set Result Set	Name Set Grid
Interference Searches					
DB=PGPB,USPT,UPAD; PLUR=YES; OP=AND					
L16		L15 not (L3 or L6 or L10 or L8)	34	L16	L16
L15		L14 and CON-S	45	L15	L15
L14		L13 and (env$)	45	L14	L14
L13		L12 and (CON-S$)	48	L13	L13
L12		L11 and (consensus or ancestral)	25969	L12	L12
L11		(HIV$ or (human immunodeficiency virus))	104532	L11	L11
L10		L9 not (L3 or L6)	7	L10	L10
L9		hahn.in. and beatrice.in.	15	L9	L9
L8		L7 not (L3 or L6)	8	L8	L8
L7		korber.in. and bette.in.	10	L7	L7
L6		L5 not L3	6	L6	L6
L5		L4 and (consensus or ancestral)	8	L5	L5
L4		gao.in. and feng.in.	242	L4	L4
L3		L2 and CON-S$	10	L3	L3
L2		L1 and (consensus or ancestral)	35	L2	L2
L1		haynes.in. and barton.in.	67	L1	L1

END OF SEARCH HISTORY

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     FILE 'WPIDS' ENTERED AT 11:53:27 ON 16 DEC 2010
                E HAYNES B F/IN
L1           65 S E3
                E HAYNES B/IN
L2           38 S E3
L3           90 S L1 OR L2
L4           50 S L3 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L5            5 S L4 AND (CONSENSUS OR ANCESTRAL)
                E GAO F/IN
L6         1996 S E3
L7           10 S L6 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L8            7 S L7 NOT L5
L9            0 S L8 AND (CONSENSUS OR ANCESTRAL)
                E KORBER B T/IN
L10           9 S E2 OR E3
                E HAHN B H/IN
L11          15 S E3
                E HAHN B/IN
L12         155 S E3
L13         166 S L11 OR L12
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L14          10 S L13 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L15       35091 S (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L16         370 S L15 AND (CONSENSUS OR ANCESTRAL)
L17          71 S L16 AND ENV?
L18           1 S L17 AND (CON-S)

     FILE 'MEDLINE' ENTERED AT 11:56:38 ON 16 DEC 2010
                 E HAYNES B/AU
L19          56 S E3
                 E HAYNES B F/AU
L20         260 S E3
L21         316 S L19 OR L20
L22          53 S L21 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L23           0 S L22 AND (CONSENSUS OR ANCESTRAL)
L24           0 S L22 AND (CON-S)
L25          22 S L22 AND (ENV?)
                 E GAO F/AU
L26         306 S E3
                 E GAO FENG/AU
L27         699 S E3
L28        1005 S L26 OR L27
L29          80 S L28 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L30          15 S L29 AND (CONSENSUS OR ANCESTRAL)
                 E KORBER B T/AU
L31         141 S E3-E6
L32         132 S L31 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L33          65 S L32 AND ENV?
L34           2 S L33 AND (CON-S)
                 E HAHN B H/AU
L35         208 S E3
                 E HAHN BEATRICE H/AU
L36          91 S E3
                 E HAHN B/AU
L37          88 S E3
L38         387 S L35 OR L36 OR L37
L39         175 S L38 AND (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L40          23 S L39 AND (CONSENSUS OR ANCESTRAL)
L41          17 S L40 AND ENV?
L42           4 S L41 NOT L30
L43      222604 S (HIV? OR HUMAN IMMUNODEFICIENCY VIRUS)
L44           9 S L43 AND (CON-S)
L45        2017 S L43 AND (CONSENSUS OR ANCESTRAL)
L46         502 S L45 AND ENV?
L47          70 S L46 AND (FUSION OR CLEAVAGE)
L48          48 S L47 AND PY<2004
L49          40 S L48 AND (CONSENSUS/AB OR ANCESTRAL/AB)
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CON-S is consensus group M polypeptide obtained from the Los Alamos 2000 sequence listing; it contains a deletion of the fusion domain (~ aa 475-505) and a C-terminal stop codon at ~aa 645.

Consensus *env* gene is constructed by generating consensus sequences of *env* genes for each subtype of a particular group (e.g., group M comprises subtypes A-D, F-H, J, and K) from the Los Alamos HIV sequence database. A consensus sequence of all subtype consensuses can be generated to avoid heavily sequenced subtypes. [p. 38]

CON-S was derived from the year 2000 database group M *env* sequences. [p. 40]

Con-S gp140 induced robust neutralization responses in multiple group M subtypes (e.g., B and C).

CON-S was obtained by aligning the consensus *env* sequences of group M subtypes (A-D, F-H, J, and K) from the 2003 Los Alamos sequence listing to obtain a parent sequence. The hypervariable regions (excluding V3) were generated through hand alignments of potential N-linked glycosylation sites and cysteine residues. The hypervariable loops tended to comprise a shorter range of lengths as compared to natural strains. The CON-S *env* gene was generated by converting amino acid sequences of CON-S to nucleotide sequences employing the codon usage of highly expressed human genes. HIV-1 gp140 Envs with deletion of the cleavage (C) site and fusion (F) domain were designated gp140ΔCF.

Fig. 29A

CON_OF_CON-S-2003 (829 a.a.)

MRVMGIQRNCQHLWRWGILIFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEIVL
ENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVYALFYKL
DVVPIDDNNSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSL
AEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISRTKWNKTLQQVAKKLRE
HFNKTIIFNPSSGGDLEITTHSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMYAPPIEGKIRCTSNIT
GLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVEREKRAVGIGAVFLGFLGAAGSTMGAASITL
TVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEI
WDNMTWMEWDKEINNYTDIIYSLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRIVFAVLSIVNR
VRQGYSPLSFQTLIPNPRGPDRPEGIEEEGGEQDRDRSIRLVNGFLALAWDDLRSLCLFSYHRLRDLILIAARTVELLGRRGWEA
LKYLWNLLQYWGQELKNSAISLLDTTAIAVAEGTDRVIEVVQRVCRAILNIPRRIRQGFERALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

Fig. 29B

CON-S-2003 140CF.pep (620 a.a.).
Nick name: 006

MRVMGIQRNCQHLWRWGILIFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEIVL
ENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVYALFYKL
DVVPIDDNNSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSL
AEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISRTKWNKTLQQVAKKLRE
HFNKTIIFNPSSGGDLEITTHSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMYAPPIEGKIRCTSNIT
GLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAK**TLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTV**
WGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEIWDNMTWMEWDKEINNYTDIIYSLIEESQNQQEK
NEQELLALDKWASLWNWFDITNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

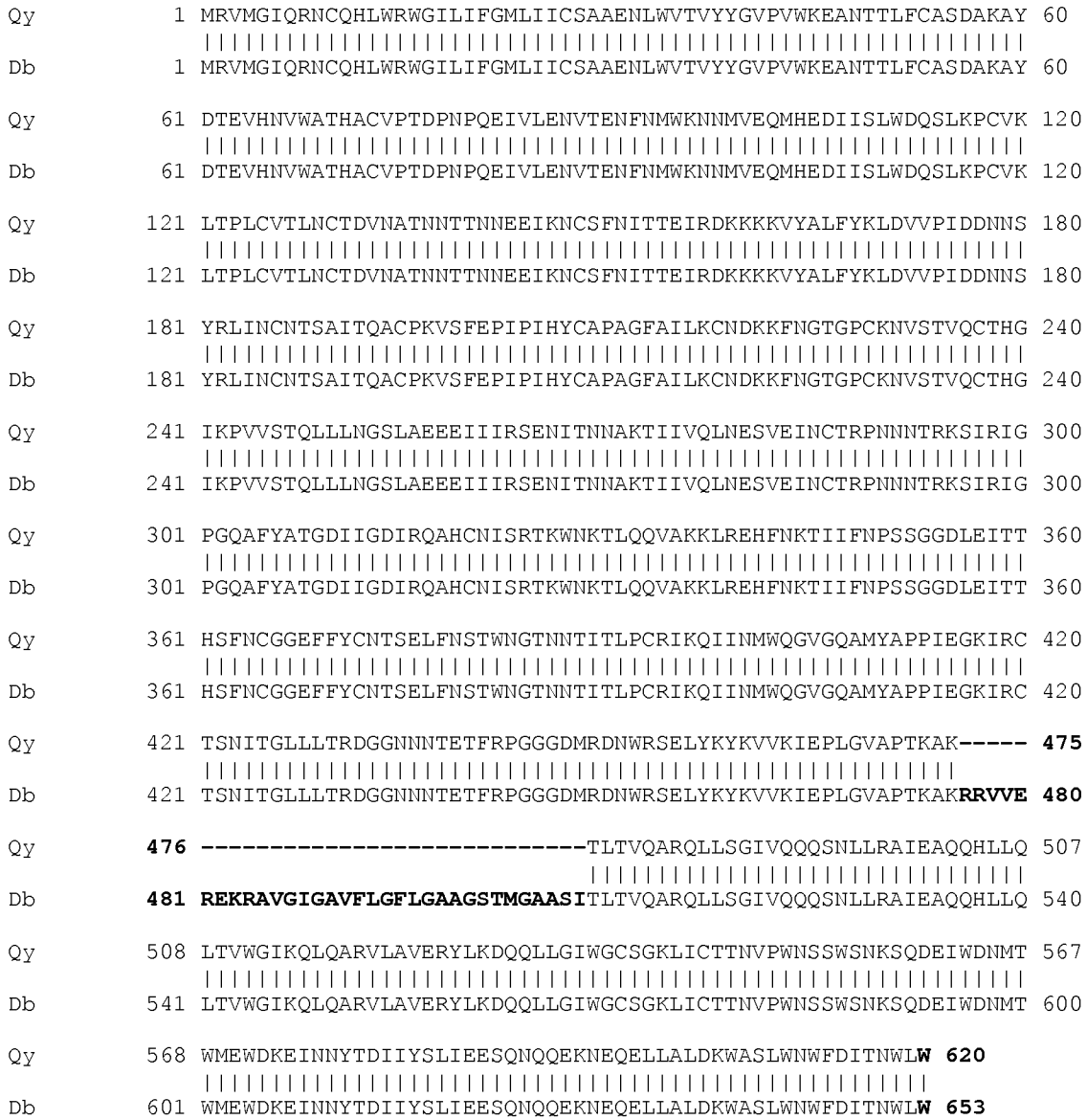
Fig. 29C

CODON-OPTIMIZED CON-S-2003 140CF.seq (1891 nt
Nick name :006

TTCAGTCGACAGCCACCATGCGGGTCATGGGGATACAGAGGAATTGCCAGCACTTGTGGAGGTGGGGAATTTTGATATTCGGGAT
GCTCATAATCTGCTCTGCCGCTGAGAACCTGTGGGTCACTGTGTATTACGGCGTTCCCGTCTGGAAAGAAGCTAATACTACCCTG
TTTTGTGCAAGCGACGCCAAAGCATACGACACCGAAGTCCACAATGTCTGGGCTACCCACGCCTGTGTACCTACTGATCCAAATC
CCCAGGAAATTGTTCTTGAAAACGTAACGGAAAACTTTAACATGTGGAAGAATAATATGGTGGAGCAAATGCACGAGGATATAAT
CAGCCTGTGGGACCAGTCCCTCAAACCATGCGTTAAACTCACTCCACTCTGCGTGACTCTGAACTGTACCGACGTGAACGCAACC
AATAATACAACAAACAATGAGGAGATAAAGAATTGTTCATTTAATATAACCACTGAGATACGGGATAAGAAAAAAAAGGTTTATG
CACTCTTTTACAAGCTCGACGTGGTGCCCATAGACGACAATAATAGCTACCGACTCATTAATTGCAATAGTAGCGCTATAACCCA
GGCATGCCCCAAAGTTTCCTTCGAGCCCATACCGATTCACTACTGCGCACCCGCCGGATTCGCCATTCTTAAATGCAATGACAAG
AAGTTCAACGGCACCGGACCCTGTAAGAACGTAAGCACTGTTCAATGTACACATGGAATTAAGCCGGTAGTGTCAACGCAGCTCC
TCCTCAACGGAAGCCTTGCAGAAGAAGAGATCATTATCAGGTCAGAAAATATCACTAACAACGCGAAAACAATCATTGTTCAGCT
GAATGAGTCTGTAGAAATCAATTGTACCCGCCCTAATAATAACACAAGAAAGTCAATTAGGATCGGACCGGCCAGGCTTTCTAC
GCAACCGGAGATATCATCGGGGATATACGACAGGCCCACTGCAACATTTCTAGAACTAAGTGGAATAAAACTTTGCAGCAGGTAG
CCAAGAAACTGCGGGAACATTTTAATAAGACAATCATCTTCAATCCAAGTAGCGGAGGGGACCTGGAAATCACTACACATTCCTT
TAACTGTGGGGGCGAGTTTTTCTACTGTAATACCTCTGAACTGTTCAACTCAACATGGAATGGCACTAAGAATACTATAACTCTT
CCTTGCAGAATAAAACAGATTATCAACATGTGGCAGGGTGTGGGGCAAGCAATGTATGCACCACCAATCGAAGGCAAAATAAGAT
GCACCTCCAATATTACCGGACTCCTCCTGACACGGGATGGCGGAAACAATAACACGGAGACCTTTAGGCCAGGCGGCGGCGATAT
GAGAGATAACTGGCGCTCCGAGCTCTATAAATACAAAGTCGTTAAGATCGAGCCCCTTGGAGTTGCGCCAACCAAAGCTAAAACC
TTGACCGTGCAAGCCAGGCAGTTGTTGTCAGGTATCGTACAGCAGCAATCTAATCTTTTGAGAGCCATTGAGGCTCAGCAGCACC
TCTTGCAGCTTACCGTCTGGGGCATCAAACAACTTCAGGCACGCGTCCTGGCCGTAGAGCGCTATTTGAAAGACCAACAACTTCT
CGGGATCTGGGGGTGTTCTGGAAAATTGATCTGCACGACAAATGTGCCTTGGAACAGCAGCTGGTCAAATAAAAGCCAAGACGAA
ATATGGGATAACATGACATGGATGGAATGGGATAAAGAAATTAATAATTACACTGACATTATTTACTCACTTATCGAGGAATCAC
AAAATCAACAGGAAAAAAATGAACAGGAACTCTTGGCTCTGGACAAATGGGCTTCACTGTGGAACTGGTTCGACATCACAAATTG
GCTCTGGTAAAGATCTTACAA

CC The invention describes an isolated protein (I) selected from 106 fully
CC defined 500-866 amino acid sequences given in the specification. Also
CC described are: a nucleic acid comprising: a nucleotide sequence encoding
CC CON6 HIV gp160 protein, subtype C ancestral HIV envelope protein, subtype
CC C consensus HIV envelope protein, subtype C consensus HIV gag protein,
CC subtype C consensus HIV nef protein, Group M consensus HIV envelope
CC protein, subtype A consensus HIV envelope protein, Group M consensus HIV
CC gag protein, Group M consensus HIV pol protein, Group M consensus HIV nef
CC protein, subtype C consensus HIV pol protein, subtype B consensus HIV gag
CC protein, or subtype B consensus HIV envelope protein, where the
CC nucleotide sequence comprises codons optimized for expression in human
CC cells; a nucleotide sequence encoding (I); or a nucleotide sequence
CC selected from 89 fully defined 633-2607 bp sequences given in the
CC specification; a vector comprising the nucleic acid of (1); a composition
CC comprising at least one protein or nucleic acid above and a carrier; and
CC inducing an immune response in a mammal. The protein is a consensus or
CC ancestral immunogen useful for inducing antibodies that neutralize a wide
CC spectrum of HIV primary isolates and/or that induces a T cell response.
CC This is the amino acid sequence of HIV CON-S env protein.
XX
SQ Sequence 829 AA;

Query Match 99.2%; Score 3338.5; DB 2; Length 829;
Best Local Similarity 94.9%;
Matches 620; Conservative 0; Mismatches 0; Indels 33; Gaps 1;


Qy 1 MRVMGIQRNCQHLWRWGILIFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAY 60
Db 1 MRVMGIQRNCQHLWRWGILIFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAY 60
Qy 61 DTEVHNVWATHACVPTDPNPQEIVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVK 120
Db 61 DTEVHNVWATHACVPTDPNPQEIVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVK 120
Qy 121 LTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVYALFYKLDVVPIDDNNS 180
Db 121 LTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVYALFYKLDVVPIDDNNS 180
Qy 181 YRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHG 240
Db 181 YRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHG 240
Qy 241 IKPVVSTQLLLNGSLAEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIG 300
Db 241 IKPVVSTQLLLNGSLAEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIG 300
Qy 301 PGQAFYATGDIIGDIRQAHCNISRTKWNKTLQQVAKKLREHFNKTIIFNPSSGGDLEITT 360
Db 301 PGQAFYATGDIIGDIRQAHCNISRTKWNKTLQQVAKKLREHFNKTIIFNPSSGGDLEITT 360
Qy 361 HSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMYAPPIEGKIRC 420
Db 361 HSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMYAPPIEGKIRC 420
Qy 421 TSNITGLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAK----- 475
Db 421 TSNITGLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVE 480
Qy 476 ----------TLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQ 507
Db 481 REKRAVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQ 540
Qy 508 LTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEIWDNMT 567
Db 541 LTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEIWDNMT 600
Qy 568 WMEWDKEINNYTDIIYSLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLW 620
Db 601 WMEWDKEINNYTDIIYSLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLW 653